



SEQUENCE LISTING

<110> NAGATA, Shigekazu
TANAKA, Masato

<120> Novel Fas Ligand Derivative

<130> 1110-0266P

<140> 09/508,849

<141> 2001-03-17

<150> PCT/JP98/04187

<151> 1998-09-17

<150> JP 9-252541

<151> 1997-09-17

<160> 17

<170> PatentIn version 3.2

<210> 1

<211> 258

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:amino acids at
111-133 from N terminal are deleted from natural
human Fas ligand

<400> 1

Met Gln Gln Pro Phe Asn Tyr Pro Tyr Pro Gln Ile Tyr Trp Val Asp
1 5 10 15

Ser Ser Ala Ser Ser Pro Trp Ala Pro Pro Gly Thr Val Leu Pro Cys
20 25 30

Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro Pro
35 40 45

Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Leu Pro
50 55 60

Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly
65 70 75 80

Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
85 90 95

Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Pro Ser
100 105 110

Pro Pro Pro Glu Lys Lys Glu Leu Arg Lys Val Ala His Leu Thr Gly
115 120 125

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Lys Ser Asn Ser Arg Ser Met Pro Leu Glu Trp Glu Asp Thr Tyr Gly
 130 135 140
 Ile Val Leu Leu Ser Gly Val Lys Tyr Lys Lys Gly Gly Leu Val Ile
 145 150 155 160
 Asn Glu Thr Gly Leu Tyr Phe Val Tyr Ser Lys Val Tyr Phe Arg Gly
 165 170 175
 Gln Ser Cys Asn Asn Leu Pro Leu Ser His Lys Val Tyr Met Arg Asn
 180 185 190
 Ser Lys Tyr Pro Gln Asp Leu Val Met Met Glu Gly Lys Met Met Ser
 195 200 205
 Tyr Cys Thr Thr Gly Gln Met Trp Ala Arg Ser Ser Tyr Leu Gly Ala
 210 215 220
 Val Phe Asn Leu Thr Ser Ala Asp His Leu Tyr Val Asn Val Ser Glu
 225 230 235 240
 Leu Ser Leu Val Asn Phe Glu Glu Ser Gln Thr Phe Phe Gly Leu Tyr
 245 250 255
 Lys Leu

<210> 2
 <211> 277
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:amino acids at
 128-131 from N terminal are deleted from natural
 human Fas ligand

<400> 2
 Met Gln Gln Pro Phe Asn Tyr Pro Tyr Pro Gln Ile Tyr Trp Val Asp
 1 5 10 15
 Ser Ser Ala Ser Ser Pro Trp Ala Pro Pro Gly Thr Val Leu Pro Cys
 20 25 30
 Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro Pro
 35 40 45
 Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Leu Pro
 50 55 60
 Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly
 65 70 75 80
 Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
 85 90 95

Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Leu Ala
 100 105 110
 Glu Leu Arg Glu Ser Thr Ser Gln Met His Thr Ala Ser Ser Leu Gly
 115 120 125
 His Pro Ser Pro Pro Pro Glu Lys Lys Glu Leu Arg Lys Val Ala His
 130 135 140
 Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu Glu Trp Glu Asp
 145 150 155 160
 Thr Tyr Gly Ile Val Leu Leu Ser Gly Val Lys Tyr Lys Lys Gly Gly
 165 170 175
 Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr Ser Lys Val Tyr
 180 185 190
 Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser His Lys Val Tyr
 195 200 205
 Met Arg Asn Ser Lys Tyr Pro Gln Asp Leu Val Met Met Glu Gly Lys
 210 215 220
 Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala Arg Ser Ser Tyr
 225 230 235 240
 Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His Leu Tyr Val Asn
 245 250 255
 Val Ser Glu Leu Ser Leu Val Asn Phe Glu Glu Ser Gln Thr Phe Phe
 260 265 270
 Gly Leu Tyr Lys Leu
 275

<210> 3
 <211> 281
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: point mutation
 of a substitution of Lys 129 for Ala from N
 terminal is present in natural human Fas ligand
 <D6>

<400> 3
 Met Gln Gln Pro Phe Asn Tyr Pro Tyr Pro Gln Ile Tyr Trp Val Asp
 1 5 10 15
 Ser Ser Ala Ser Ser Pro Trp Ala Pro Pro Gly Thr Val Leu Pro Cys
 20 25 30
 Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro Pro
 35 40 45

Pro. Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Pro Leu Pro
 50 55 60
 Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly
 65 70 75 80
 Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
 85 90 95
 Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Leu Ala
 100 105 110
 Glu Leu Arg Glu Ser Thr Ser Gln Met His Thr Ala Ser Ser Leu Glu
 115 120 125
 Ala Gln Ile Gly His Pro Ser Pro Pro Pro Glu Lys Lys Glu Leu Arg
 130 135 140
 Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu
 145 150 155 160
 Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly Val Lys Tyr
 165 170 175
 Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr
 180 185 190
 Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser
 195 200 205
 His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln Asp Leu Val Met
 210 215 220
 Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala
 225 230 235 240
 Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His
 245 250 255
 Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe Glu Glu Ser
 260 265 270
 Gln Thr Phe Phe Gly Leu Tyr Lys Leu
 275 280

<210> 4

<211> 774

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:DNA coding for
amino acids SEQ ID No.1

<400> 4

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atgcagcagc ccttcaatta cccatatccc cagatctact gggtaggacag cagtgccagc 60
tctccctggg cccctccagg cacagttctt ccctgtccaa cctctgtgcc cagaaggcct 120
gggtcaaagga ggccaccacc accaccgcca ccgccaccac taccacctcc gccgccgccg 180
ccaccactgc ctccactacc gctgccaccc ctgaagaaga gaggaacca cagcacaggc 240
ctgtgtctcc ttgtgatgtt ttcatgggtt ctggttgccct tggtaggatt gggcctgggg 300
atgtttcagc tcttccacct acagaaggag cccagtcacac cccctgaaaa aaaggagctg 360
aggaaagtgg cccatttaac aggcaagtcc aactcaaggt ccatgcctct ggaatgggaa 420
gacacctatg gaattgtcct gctttctgga gtgaagtata agaagggtgg ccttgtgatc 480
aatgaaactg ggctgtactt tgtatatccc aaagtatact tccgggggtca atcttgcaac 540
aacctgcccc tgagccacaa ggtctacatg aggaactcta agtatcccca ggatctgggtg 600
atgatggagg ggaagatgat gagctactgc actactgggc agatgtgggc ccgcagcagc 660
tacctggggg cagtgttcaa tcttaccagt gctgatcatt tatatgtcaa cgtatctgag 720
ctctctctgg tcaattttga ggaatctcag acgtttttcg gcttatataa gctc 774

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<210> 5

<211> 831

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:DNA coding for
amino acids SEQ ID No.2

<400> 5

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atgcagcagc ccttcaatta cccatatccc cagatctact gggtaggacag cagtgccagc 60
tctccctggg cccctccagg cacagttctt ccctgtccaa cctctgtgcc cagaaggcct 120
gggtcaaagga ggccaccacc accaccgcca ccgccaccac taccacctcc gccgccgccg 180
ccaccactgc ctccactacc gctgccaccc ctgaagaaga gaggaacca cagcacaggc 240
ctgtgtctcc ttgtgatgtt ttcatgggtt ctggttgccct tggtaggatt gggcctgggg 300
atgtttcagc tcttccacct acagaaggag ctggcagaac tccgagagtc taccagccag 360
atgcacacag catcatcttt gggccacccc agtccacccc ctgaaaaaaa ggagctgagg 420
aaagtggccc atttaacagg caagtccaac tcaagggtcca tgcctctgga atgggaagac 480
acctatggaa ttgtcctgct ttctggagtg aagtataaga aggggtggcct tgtgatcaat 540
gaaactgggc tgtactttgt atattccaaa gtatacttcc ggggtcaatc ttgcaacaac 600
ctgcccctga gccacaaggt ctacatgagg aactctaagt atccccagga tctgggtgatg 660
atggagggga agatgatgag ctactgcact actgggcaga tgtgggcccg cagcagctac 720
ctggggggcag tgttcaatct taccagtgtg gatcatttat atgtcaacgt atctgagctc 780
tctctgggtca attttgagga atctcagacg tttttcggct tatataagct c 831

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<210> 6

<211> 843

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:DNA coding for
amino acids SEQ ID No.3

<400> 6

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atgcagcagc ccttcaatta cccatatccc cagatctact gggtaggacag cagtgccagc 60
tctccctggg cccctccagg cacagttctt ccctgtccaa cctctgtgcc cagaaggcct 120
gggtcaaagga ggccaccacc accaccgcca ccgccaccac taccacctcc gccgccgccg 180
ccaccactgc ctccactacc gctgccaccc ctgaagaaga gaggaacca cagcacaggc 240
ctgtgtctcc ttgtgatgtt ttcatgggtt ctggttgccct tggtaggatt gggcctgggg 300
atgtttcagc tcttccacct acagaaggag ctggcagaac tccgagagtc taccagccag 360

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atgcacacag catcatcttt ggaggcacia ataggccacc ccagtcacc cctgaaaaa 420
aaggagctga ggaaagtggc ccatttaaca ggcaagtcca actcaaggtc catgcctctg 480
gaatgggaag acacctatgg aattgtcctg ctttctggag tgaagtataa gaaggggtggc 540
cttgtgatca atgaaactgg gctgtacttt gtatattcca aagtatactt ccgggggtcaa 600
tcttgcaaca acctgcccct gagccacaag gtctacatga ggaactctaa gtatccccag 660
gatctggtga tgatggaggg gaagatgatg agctactgca ctactgggca gatgtggggc 720
cgcagcagct acctgggggg agtgttcaat cttaccagtg ctgatcattt atatgtcaac 780
gtatctgagc tctctctggt caattttgag gaatctcaga cgtttttcgg cttatataag 840
ctc 843

<210> 7
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:a sense primer
BOS6

<400> 7
cctcagacag tggttcaaag 20

<210> 8
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:an antisense
deletion primer DA4

<400> 8
ttttcagggg gtggactggg ctcccttctgt aggtggaag 39

<210> 9
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:HFLP3

<400> 9
gctctagaac attctcggtg cctgtaac 28

<210> 10
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:DA5

<400> 10

tggactggggg tggcccaaag atgatgctgt

30

<210> 11

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:DA6

<400> 11

ggggtggcct atttgtgcct ccaaagatga tgc

33

<210> 12

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:sequence of
human FasL from amino acids 130 to137

<400> 12

Gln Ile Gly His Pro Ser Pro Pro

1

5

<210> 13

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:the amino acid
sequence around the cleavage site of FasL

<400> 13

Glu Lys Gln Ile

1

<210> 14

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:the cleavage
site of THN-alpha

<400> 14

Leu Ala Gln Ala Val Arg Ser Ser

1

5

F1
wt

<210> 15
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:the cleavage
 site of CD40

<400> 15
 Asn Ser Phe Glu Met Gln Lys Gly
 1 5

<210> 16
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:the cleavage
 site of FasL

<400> 16
 Ser Leu Glu Lys Gln Ile Gly His
 1 5

<210> 17
 <211> 281
 <212> PRT
 <213> Homo sapiens

<400> 17
 Met Gln Gln Pro Phe Asn Tyr Pro Tyr Pro Gln Ile Tyr Trp Val Asp
 1 5 10 15
 Ser Ser Ala Ser Ser Pro Trp Ala Pro Pro Gly Thr Val Leu Pro Cys
 20 25 30
 Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro Pro
 35 40 45
 Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Leu Pro
 50 55 60
 Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly
 65 70 75 80
 Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
 85 90 95
 Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Leu Ala
 100 105 110
 Glu Leu Arg Glu Ser Thr Ser Gln Met His Thr Ala Ser Ser Leu Glu

115							120					125				
Lys	Gln	Ile	Gly	His	Pro	Ser	Pro	Pro	Pro	Glu	Lys	Lys	Glu	Leu	Arg	
130						135					140					
Lys	Val	Ala	His	Leu	Thr	Gly	Lys	Ser	Asn	Ser	Arg	Ser	Met	Pro	Leu	
145					150					155					160	
Glu	Trp	Glu	Asp	Thr	Tyr	Gly	Ile	Val	Leu	Leu	Ser	Gly	Val	Lys	Tyr	
				165					170					175		
Lys	Lys	Gly	Gly	Leu	Val	Ile	Asn	Glu	Thr	Gly	Leu	Tyr	Phe	Val	Tyr	
		180						185					190			
Ser	Lys	Val	Tyr	Phe	Arg	Gly	Gln	Ser	Cys	Asn	Asn	Leu	Pro	Leu	Ser	
		195					200					205				
His	Lys	Val	Tyr	Met	Arg	Asn	Ser	Lys	Tyr	Pro	Gln	Asp	Leu	Val	Met	
		210				215					220					
Met	Glu	Gly	Lys	Met	Met	Ser	Tyr	Cys	Thr	Thr	Gly	Gln	Met	Trp	Ala	
225					230					235					240	
Arg	Ser	Ser	Tyr	Leu	Gly	Ala	Val	Phe	Asn	Leu	Thr	Ser	Ala	Asp	His	
				245					250					255		
Leu	Tyr	Val	Asn	Val	Ser	Glu	Leu	Ser	Leu	Val	Asn	Phe	Glu	Glu	Ser	
			260					265					270			
Gln	Thr	Phe	Phe	Gly	Leu	Tyr	Lys	Leu								
		275					280									